Remarks

A. Status of the Claims

Claims 1-12 were pending at the time the Advisory Action was mailed. Claims 1-5 have been amended. Support for these amendments can be found throughout the specification and claims as originally filed, as described below. Claim 10 is cancelled. No new matter is added.

Claims 1-9, 11, and 12 are pending.

B. Summary of Interview

On August 23, 2007, Applicant's representative, Michael R. Krawzsenek, spoke with Examiner Frank Choi about the pending claims in this case. As discussed, Applicant has revised the current claims to be substantially similar to claims allowed in the corresponding Canadian case (Canadian patent 2,406,592, which issued on September 30, 2003). At the request of Examiner Choi, Applicant provides a copy of the prosecution history of the '592 patent as Appendix A.

C. The Written Description Rejection Is Overcome

Claims 1-12 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Specifically, the Examiner contends that the phrase "distinct mean particle sizes" is not supported in Applicant's specification.

Applicant respectfully disagrees. The specification and claims provide the necessary written description support for this phrase pursuant to 35 U.S.C. §112, first paragraph. However, in an effort to further the prosecution and secure prompt allowance in this case, the claims have been amended to specify that Pyridoxine HCl and Doxylamine Succinate active ingredients are provided in the form of powders having different granular sizes, as found in the text of the originally-filed specification. *See, e.g.*, paragraphs [0003] and [0020].

A person of skill in the art would "reasonably conclude" from the specification that Applicant was in possession of the invention as presently defined in the claims at the time the application was filed. MPEP § 2163. For example, paragraph [0003] of the specification explains that the active ingredients of Diclectin®, namely Doxylamine Succinate and Pyridoxine HCl, are obtained in the form of powders having different granular sizes, which poses, for example, a content uniformity challenge during the manufacture of dosage forms with such active ingredients. Paragraph [0020] of the specification explains that the problems associated with these "size difference[s]" are solved by the present invention.

For at least these reasons, Applicant respectfully requests that the written description rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

D. The Obviousness Rejection Is Overcome

Claims 1-12 are rejected under 35 U.S.C. § 103(a) as being obvious over Chen (U.S. Pat. No. 5,260,069) in view of Chu *et al.* (U.S. Pat. No. 6,419,954) and Bishai *et al.* In summary, the Examiner contends that the primary reference, Chen, "...discloses a process for preparation of pulsatile particles which can contain combinations of therapeutic agents in which the granule containing the active agents and swelling agent are prepared by the well known and economic roller compaction method." Office Action dated December 15, 2006 at pp 2-3. As for Chu *et al.*, it is relied upon for apparently disclosing "...embodiments in which a tablet can further include untreated active agents (*e.g.*, without coating material or powders) in addition to the active agent containing particles and that the active agent particles can contain vitamins or drugs...." *Id.* Bishai *et al.* is cited as disclosing "...the combination of 10 mg doxylamine succinate and 10 mg pyridoxine HCl is safe and effective in treating nausea and vomiting associated with pregnancy." *Id.* at page 3.

The Examiner concedes that the cited art fails to "disclose the use of more than one active ingredient, such as the combination of doxylamine succinate and pyridoxine HCl." *Id.* In an effort to supplement the deficiencies of the prior art, the Examiner contends that a person of ordinary skill in the art "...would have been motivated to modify the prior art as above with the expectation that the combination of doxylamine succinate and pyridoxine in granules prepared by roller compaction and sieving to obtain appropriate mesh size would be safe and effective in treating NVP." *Id.*

Applicant respectfully disagrees. The claims prior to any amendment were not rendered obvious by the cited references. However, in an effort to further prosecution and secure prompt allowance in this case, claims 1-5 have been amended to specify that the pharmaceutical dosage forms prepared by the claimed method comprise Pyridoxine HCl and Doxylamine Succinate as active ingredients. Claims 1-5 additionally comprise the following: "(a) providing said Pyridoxine HCl and Doxylamine Succinate active ingredients in the form of powders having different granular sizes." Support for these amendments may be found in the specification and originally-filed claims, as described above. The present claims are not obvious over the cited art for at least the following reasons.

1. The Prior Art Fails to Disclose "providing said Pyridoxine HCl and Doxylamine Succinate active ingredients in the form of powders having different granular sizes"

The recent *KSR v. Teleflex* Supreme Court decision did not change the requirement that to support an obviousness rejection, a reference, alone or in combination, must teach or suggest every element of a claimed invention. MPEP § 2143. At a minimum, the cited references fail to teach step (a) recited in independent claims 1-5: "providing said Pyridoxine HCl and Doxylamine Succinate active ingredients in the form of powders having different granular sizes." As such, the obviousness rejection cannot stand.

Chen *et al.* generally disclose pulsatile dosage forms comprising a plurality of populations of pellets enclosed within a capsule or tablet, wherein the individual pellets are composed of a core containing a drug and a swelling agent, the core being enclosed in a membrane having specific properties towards water. *See* Chen *et al.*, Abstract. Chen *et al.* also disclose that the methods for preparing such pulsatile dosage forms may employ any conventional pharmaceutical equipment and products, and that the core of the pellets may be prepared by roller compaction. *See, e.g., id.* at col. 1, lines 56-68 and col. 2, lines 60-65. However, the provision of active ingredients in the form of powders having different granular sizes is not discussed.

Chu *et al.* generally disclose a tablet comprising a gel-forming material and at least one particle comprising an active agent in contact with a coating material to modify release of the active agent. *See* Chu *et al.*, Abstract. Chu *et al.* further disclose that any suitable granulation method can be used to produce particles comprising an active agent, such as roller compaction. *See, e.g., id.* at col. 12 lines, 25-44. No discussion regarding active agents in powder form having different granular sizes is found in this reference.

As for Bishai *et al.*, it appears to disclose that a combination of both doxylamine succinate and pyridoxine hydrochloride (as found in Diclectin™) is safe and effective in the treatment of nausea and vomiting during pregnancy. *See, e.g.*, Bishai *et al.* at pp 167, 170 and 173-177. However, Bishai *et al.* fail to disclose or suggest any aspect of a manufacturing method for preparing a formulation including these active ingredients—much less Applicant's claimed method of providing these "active ingredients in the form of powders having different granular sizes."

Each of the cited references fail to disclose or even suggest Applicant's method for the preparation of pharmaceutical dosage forms comprising Pyridoxine HCl and Doxylamine Succinate as active ingredients, wherein the active ingredients are initially provided in the form of powders having different granular sizes. Further, Applicant respectfully notes that the combination of the cited references also fails to disclose or even suggest (1) the technical problem of having Pyridoxine HCl and Doxylamine Succinate as active ingredients provided in the form of powders having different granular sizes involved in a method of preparation of a pharmaceutical dosage form, let alone (2) the method used and claimed by the Applicant to solve that technical problem. This alone overcomes the obviousness objection. MPEP § 2143.03.

2. There Is No Apparent Reason to Modify the Cited References to Arrive at the Present Invention

The *KSR* Court explained the importance of "identify[ing] a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. slip op. at 14-15 (2007). The Court noted that there should be an "explicit" analysis regarding "whether there was an **apparent reason** to combine the known elements **in the fashion claimed** by the patent at issue." *Id.* at 14 (emphasis added). An apparent reason for combining the elements of Chu *et al.*, Chen *et al.* and Bishai *et al.* in the fashion claimed by Applicant does not appear to exist for at least the reasons discussed above.

3. Additional Considerations

Applicant reiterates that the presently claimed roller compacting method provided surprising and unexpected results as to alleviation of ingredient loss during manufacturing of pharmaceutical dosage forms comprising Pyridoxine HCl and Doxylamine Succinate as active ingredients, wherein such active ingredients are provided in the form of powders having different

granular sizes. This method also resulted in beneficial content uniformity of such active ingredients. *See, e.g.*, Specification at page 5, paragraph [0014]. These unexpected results are clearly apparent from the comparison between example 1 (prior art, starting on page 7, paragraph [0022] of Applicant's specification) and example 2 (invention, starting on page 9, paragraph [0025] of Applicant's specification), which were conducted using Pyridoxine HCl and Doxylamine Succinate as powdered active ingredients having different granular sizes (*see id.* at page 1-2, [0003], [0004], [0020]). As these Examples employed Pyridoxine HCl and Doxylamine Succinate as powdered active ingredients having different granular sizes, the unexpected results obtained in these experiments are commensurate with the scope of the claims in accordance with MPEP § 716.02(d).

To discount the significance of these results, the Examiner cites *Pfizer Inc. v. Apotex, Inc.*, 480 F.3d 1348 (Fed. Cir. 2007) for the proposition that "creating a process that is more desirable for example because it is more efficient is universal, and even common sensical." Advisory Action, page 2. However, this statement is taken out of context. Prior to making this statement, the *Pfizer* court cautioned that "[I]n order to properly evaluate whether a superior property was unexpected, the court [below] should have considered what properties were expected." 480 F.3d at 1371. Indeed, Pfizer's case failed because the record was "devoid of any evidence of what the skilled artisan would have expected." *Id.*

By comparison to the facts in *Pfizer*, Applicant's specification explains that "[i]t is observed that due to their small size and possible electrostatic charge, Pyridoxine HCl particles tend to easily adhere to manufacturing vessels and other processing or storage equipment." Specification at page 2, paragraph [0004]. As a roller compactor is a piece of processing equipment, one of skill in the art would have expected that this machine, too, would have

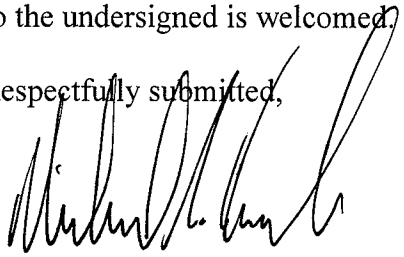
suffered from detrimental Pyridoxine HCl particle adherence. However, as explained above, such product loss was *dramatically lowered* when a roller compactor was used, in comparison to when the prior art method was used. *See also, e.g.* specification at page 10, paragraph [0028]. Therefore, these results were surprising and unexpected.

Accordingly, even if a *prima facie* case of obviousness has been established by the Examiner, which Applicant does not concede, the obviousness rejection cannot stand in view of this secondary consideration. *See* MPEP 2141; *see also In re Pravin*, 54 F.3d 746, 750 (Fed. Cir. 1995) ("One way for a patent applicant to rebut a prima facie case of obviousness is to make a showing of 'unexpected results,' *i.e.*, to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected.").

E. Conclusion

Applicant believes that the present document is a full and complete response to the Advisory Action dated June 15, 2007, but faxed to Applicant on June 12, 2007. Applicant submits that the claims are in condition for allowance, and an early indication to that effect is solicited. If the Examiner has any questions or any suggestions that will help the application proceed more quickly to allowance, a telephone call to the undersigned is welcomed.

Respectfully submitted,



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